

REMARKS

The Office Action dated May 7, 2002, has been received and reviewed. Claims 1-9 and 36 are pending in this application. Claim 36 has been amended. The version of the claim amendments indicating changes is appended hereto and is captioned "Version with Markings to Show Changes Made." The amendments to the specific rejections are addressed below. Applicants respectfully request reconsideration of the application as amended herein and in light of the arguments below.

I. Claim Amendments

Claim 36 has been amended to insert the word "isolated" as suggested by the Examiner.

II. Drawings

The drawings are objected to as allegedly each figure is not described separately in the Brief Description of the Drawings. Applicants note that the specification clearly delineates parts (A) and (B) of Figures 1 and 3 as well as pictures (A), (B) and (C) of figure 4 in the bolded letters within the Brief Description of the Drawings. The bolded letters specifically describe the figures in the drawings. Accordingly, Applicants respectfully request reconsideration and withdrawal of the objections to the drawings.

III. Claim Rejections – 35 U.S.C. § 101

Claim 36 stands rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter. Claim 36 has been amended to recite "an isolated oligonucleotide" to overcome this rejection as suggested by the Examiner. Accordingly, Applicants respectfully request that the 35 U.S.C. § 101 rejection be withdrawn.

IV. Claim Rejections – 35 U.S.C. § 112, second paragraph

Claims 1-9 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully disagree with this assessment.

Specifically, Claim 1 is rejected as indefinite because the "stringent conditions" are not specified. Applicants respectfully disagree with this assessment, as "stringent conditions" is a term of art commonly understood amongst those skilled in the art. In addition, stringent conditions are taught in the specification. As is disclosed in the specification on page 13, lines 31-35, page 14, lines 1-8, and page 15, lines 2-20, the "stringent conditions" referred to in Claim 1 are "conditions well known in the art" that are varied slightly in order to detect a variety of sequences. Thus, the term "stringent conditions" merely refers to conditions that allow genetic material of similar identity to hybridize, but does not and cannot delineate the precise conditions for unknown sequences and materials. *See also Synopsis of Application of Written Description Guidelines* from <http://www.uspto.gov/web/menu/written.pdf>, p. 35-37 (which uses an example that states "A nucleic acid that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO: 1" and states that "hybridization techniques using a known DNA as a probe under highly stringent conditions were conventional in the art at the time of filing."). This example used by the Patent Office indicates that the term "stringent" is recognized as a term of art and that the Patent Office finds the term to be sufficiently self-explanatory. Applicants respectfully request that the 35 U.S.C. § 112, second paragraph rejection be withdrawn.

Claim 36 is rejected for having insufficient antecedent basis. The claim has been amended to replace "a nucleic acid" with "the isolated nucleic acid" as suggested by the Examiner. Applicants respectfully request that the 35 U.S.C. § 112, second paragraph rejection be withdrawn.

Claims 2-9 are rejected for depending on an independent claim. As these claims depend from Claim 1, the clarification of the phrase "stringent conditions" in Claim 1 should address these issues for the dependent claims as well. Applicants respectfully request that the 35 U.S.C. § 112, second paragraph rejection to claims 1-9 and 36 be withdrawn.

V. Claim Rejections – 35 U.S.C. § 112, first paragraph

a. Enablement

Claims 1-9 and 36 are rejected under 35 U.S.C. § 112, first paragraph, for failing to enable a person skilled in the art to make and use the invention. Applicants respectfully disagree with this assessment.

The "test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." (MPEP §2164.01, citing *In re Wands*, 858 F.2d 731, 737). With respect to the present application, the Examiner has provided no objective evidence to doubt the veracity of Applicant's specification, or that the invention does not work as described. The Patent Office has the affirmative burden to set forth such evidence in order to establish even a *prima facie* case of non-enablement (MPEP § 2164.04; *In re Wright*, 999 F.2d 1557 (Fed. Cir. 1993); *In re Marzocchi*, 439 F.2d 220, 224 (CCPA 1971)). Thus, the rejection should be withdrawn.

The Office Action expresses concern that Applicants have not demonstrated actual reduction to practice of particular embodiments of the invention. The Applicant notes that disclosure in the specification of an actual reduction to practice is *not* necessary to satisfy the enablement requirement (*see*, MPEP §2164.02; *Gould v. Quigg*, 822 F.2d 1074, 1078; 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987)). The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with the expenditure of no more effort than is normally required in the art.

Moreover, the Court of Appeals for the Federal Circuit has held that it is not necessary for the specification or claims to list all operative embodiments, or to exclude all inoperative embodiments, stating: "even if some of the claimed combinations [are] inoperative, the claims are not necessarily invalid. It is not a function of the claims to specifically exclude ... possible inoperative substances...". *Atlas Powder Co. v. DuPont*, 750 F.2d 1569; 224 USPQ 409 (CAFC 1984). All that is required by 35 U.S.C. § 112 is that one skilled in the art may determine the inoperative embodiments with no more than routine skill. The Applicant submits that this standard is satisfied in the present application.

Applicants note that it is somewhat unclear from the first sentence of the rejection what elements of the claim are specifically objected to (lines 18-20, page 4 and lines 1-6, page 5). In particular, comments regarding DNA vectors seem inapplicable, since the claims at issue are not related to DNA vectors. The bases of this rejection, as surmised from later paragraphs of the Office Action, are as follows.¹ First, it appears from the language in the Office Action that the claims stand rejected as allegedly being overly broad and encompassing nucleic acids encoding variants that may be unrelated to the polynucleotide of SEQ ID NO: 1. Next, the claims stand rejected as allegedly the claims are single means claims. Additionally, the claims are rejected as purportedly they may encompass sequences coding for inactive or mutant proteins. The claims also allegedly fail to define a critical structural feature. Finally, the action rejects the claims on the basis that the claims allegedly are overly similar to that in *Maizel*. Each of these issues is addressed below.

Applicants respectfully disagree with the Office Action's assessment of the claims. Applicants note that Claim 1 recites an isolated nucleic acid having the sequence identified as SEQ ID NO: 1. Certainly any isolated nucleic acid which has sequence identical to that of SEQ ID NO: 1 would be of identical structure as the claimed nucleic acid and an identical function, if active. The next element of claim 1 is directed to an isolated nucleic acid that hybridizes to the complement of SEQ ID NO: 1 under stringent conditions and encodes an insulin-responsive glucose transporter. As discussed in the specification on page 15, any genetic material that is hybridizing under "stringent" conditions is of at least 75% identity to the original sequence, as is known in the art. 75% identity indicates that the two variants would have similar structure. Additionally, the claim recites the phrase "and encodes an insulin responsive glucose transporter." The use of these "stringency" and "encoding" allows one of skill in the art to know that any sequence that both has a minimum of 75% identity and encodes an insulin responsive glucose transporter would certainly have similar structure and function to SEQ ID NO: 1.

Finally, claim 1 includes a recitation wherein any nucleic acid that encodes the same glucose transporters as the sequences discussed *supra*, but contain a slightly

¹ Applicants note that if Applicants' understanding of the present rejection is erroneous, it is respectfully requested that the Examiner clarify the present rejection so that applicants may respond appropriately.

different nucleic acid sequence due to the degeneracy of the genetic code, may be within the scope of the claim. Once again, the concern that unrelated structural or functional variants would be included in this class is misplaced. First, if there is an alteration that results in a slight change in nucleic acid sequence but does not alter the amino acid sequence of the protein encoded by the nucleic acid, the structure of the altered nucleic acid is typically not fundamentally altered from that of SEQ ID NO: 1. Second, since the potential sequence containing some different nucleic acids would still encode the same amino acids, and ultimately the same protein as SEQ ID NO: 1, there would be no actual change in function. Therefore, applicants submit that the present application is enabled.

Applicant must also respectfully disagree with the Office Action's assessment that the claims are a single means claim that attempts to cover every conceivable structure. The Office Action postulates that applicant is attempting to claim "any nucleic acid that hybridizes to or encodes a glucose transporter polypeptide or fragments thereof." Claim 1 and its dependent claims are directed to any nucleic acid that hybridizes to *and* encodes a glucose transporter protein, and section (b) directs one of skill in the art to sequences that encode an insulin-responsive glucose transporter protein. Further, the claims in this application are not single means claims. According to the MPEP 2164.08(a), a single means claim occurs where a claim covers every possible means for achieving a result while the specification only discloses limited means. Here, applicant is claiming nucleic acid sequences, and does not posit any means for attaining these sequences. Because the claims are directed to an actual nucleic acid sequence, and does not extend to the methods for creating or discovering this sequence, there are no means disclosed and there can be no single means claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of the single means claim rejection.

The Office Action also states that the disclosure does not teach how to use the numerous nucleic acids that would hybridize to SEQ ID NO: 1 and encode variants lacking the critical feature of the claimed invention. Again, Applicants must respectfully refer to arguments *supra*. As previously discussed, the scope of these claims does not encompass nucleic acids of structure or function significantly different from that of the claimed SEQ ID NO: 1. Due to the recitation that all claimed nucleic acids must encode a glucose transporter, and the further recitation

that the nucleic acid must be capable of hybridizing to SEQ ID NO: 1 under stringent conditions (i.e. have over 75% homology), all nucleic acids claimed will necessarily possess the recited feature of the claimed invention. One of skill in the art would readily be able to assay the nucleic acids to determine if hybridization has occurred. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

The Office Action further objects to these claims because they may identify inactive proteins or nucleic acids containing mutations that would alter the resulting protein. However, this claim is not for an isolated nucleic acid sequence encoding an active protein; it is for a nucleic acid sequence encoding a glucose transporter protein, and in the case of (b), an insulin-responsive glucose transporter protein. Whether the resulting protein is functional or not is irrelevant. Certainly a variation in the nucleic acid sequence that results in a nonsense or missense mutation may be of more interest than SEQ ID NO: 1 by itself. The claims, as written, are not designed to claim sequences that would result in unrelated nucleic acids encoding unrelated proteins. Instead, as can be observed by the claim's recitations to nucleic acids that hybridize under stringent conditions (or are of at least 75% homology) and to nucleic acids encoding a glucose transporter protein, the claims are designed to include homologues and mutant versions of the claimed sequence that encode a glucose transporter protein. Where a sequence hybridizes to SEQ ID NO: 1 under stringent conditions, but does not produce a functional protein product, it is typically of great interest to determine the reason for this failure. Indeed, when a gene that *should* encode a glucose transporter protein instead produces no functional protein or a truncated protein, it may be of great importance in determining methods of treating illness. Thus, although the resultant protein might not function as the claimed glucose transporter protein traditionally does, the very non-functionality of the gene product can be quite useful for disease-related studies. The utility of an inactive or variant mutant in enabling a researcher to screen for disease in asymptomatic individual or allowing researchers to target the gene with gene therapy is both obvious and inherent to anyone skilled in this field. Therefore, applicants respectfully request reconsideration of the claims contained in the present application.

The Office Action next raises the issue of non-specific binding again. The position is reiterated that non-specific hybridizations to SEQ ID NO: 1 may result in

claims to unrelated nucleic acids. However, as explained *supra*, the claims are directed to the isolated nucleic acid sequence SEQ ID NO:1 or to nucleic acids with sufficient homology to the aforementioned sequence and to nucleic acids encoding a glucose transporter protein. This claim is written such that unrelated proteins will not be incorporated into this invention. Therefore, any concerns that the application fails to disclose uses for these oligonucleotides are misplaced.

The Office Action also alleges that the claims fail to reveal a "critical structural feature." However, it is widely accepted by both those schooled in the art, as well as the Patent Office itself, that where a claim recites a nucleic acid sequence, the sequence itself is the critical structural feature. For example, please see U.S. Patent 6,444,802, 6,441,270, etc. Those skilled in the art do not need further information to use the disclosed invention.

The Office Action goes on to discuss *Ex parte Maizel*, and compare the facts of this application to the *Maizel* fact pattern. 27 USPQ2d 1662 (BPAI 1992). However, the facts here are distinguishable from *Maizel*. In *Maizel*, the claim language was directed to a specific sequence "or a biologically functional equivalent thereof." *Id.* at 1663. The court objected to the use of that phrase, stating that it was "so broad as to encompass any protein regardless of structure that is 'functionally equivalent to BCGF in terms of biological activity'." *Id.* at 1665. In other words, the claim in *Maizel* incorporated not only members of the protein family and mutations of the protein, but also completely unrelated proteins that ultimately performed the same function. It was noted that the problem with this application was that the party had characterized the DNA not by "what it is but, rather, by what it does." *Id.*

In the claim at hand, Applicants claim SEQ ID NO: 1 and nucleic acids that are of high homology to the known sequence and which encode a glucose transporter protein, or isolated nucleic acids that differ based upon the degeneracy of the genetic code. This claim does not include unrelated proteins. Furthermore, unlike the claim in *Maizel*, the present claims do not contemplate becoming a single means claim, as discussed *supra*. Unlike *Maizel*, here the inclusion in the claim of the function of the claimed proteins serves not to broaden the scope of this claim, but rather to narrow it.

In summation, the genetic material encompassed by the claim is defined as sequences that (a) comprise SEQ ID NO:1 and encode a glucose transporter protein, (b) are of sufficient homology to SEQ ID NO:1 and encode an insulin-responsive

glucose transporter protein, and (c) are of a degenerate sequence that encode the same amino acid sequences as the nucleic acids claimed in (a) or (b) and encode a glucose transporter protein. This claim is not a single means claim, as it is directed to a product and not a means of producing that product; all sequences claimed are both useful and important whether they result in an active protein or not; and finally, these claims are more specific than those in *Maizel* and are simply not comparable. Accordingly, Applicants respectfully request that this 35 U.S.C. § 112, first paragraph rejection be withdrawn.

b. Lack of Written Description

Claims 1-3, 6-9, and 36 are rejected under 36 U.S.C. § 112, first paragraph, for allegedly failing to provide an adequate written description. Again, Applicants respectfully disagree with this assessment.

The claims are first rejected on the grounds that purportedly the disclosure of one polypeptide does not adequately describe the scope of the claimed genus to one skilled in the art. Applicants respectfully request reconsideration of this issue. To the contrary, these claims are actually quite specific in scope.

Under claim 1, section (b), the claim recites nucleic acids that both hybridize to SEQ ID NO:1 under stringent conditions and encode a glucose transporter protein. To an individual skilled in the art, this claim would properly and adequately describe a few relevant categories of genes. First, the claim recites to those nucleic acids binding under "stringent conditions"; based on the specification, the sequence of this claim comprises approximately 75% or better identity to SEQ ID NO: 1. This would bring to mind several embodiments to one skilled in the art: the homolog to the GLUT10 gene in other animals; variant versions of the GLUT10 sequence that have either beneficial, detrimental, or benign mutations, as well as possibly alternately expressed forms of GLUT10 in other human tissues; and members of a GLUT10 gene family. Although the claim is not limited to these specific embodiments, the scope of this claim is quite clear to one skilled in the art.

Under section (c) of claim 1, the claim may include nucleic acids that encode the same amino acid sequence as that encoded by SEQ ID NO: 1. This claim includes situations where there is a point mutation or variation that results in no actual alteration in the amino acid sequence. Such polymorphisms are useful in many regards, as they may be pivotal in evolutionary genetic studies as well as in linkage

mapping. As the resultant amino acid sequence remains unchanged, as does the function of the resulting gene product, such sequence is clearly appropriately included and described in this claim.

The Office Action next cites *Regents of the University of California v. Eli Lilly & Co.* as an example of an inadequate written description. In *Regents*, the court held that it was necessary to provide the sequence information for claimed nucleotides. However, unlike the claims in *Regents*, the claims here actually **do recite the full sequence claimed**, although every possible permutation and homologue is not disclosed. Such disclosure is unnecessary, as anyone educated in the art would readily comprehend the scope of the claim as written.

The Office Action also recites concerns that the claims will encompass unrelated structural or functional variants. This argument has primarily been addressed *supra*, when Applicants explained the full scope of the claims and the impossibility of an unrelated nucleic acid sequence falling within the bounds of this claim. *See supra*.

In addition, the Office Action cites concerns that the application lacks guidance regarding the production of mutants and that allegedly there is no description of sites within the sequence that can tolerate variability. Certainly this is simply well known, basic knowledge among those skilled in the art. There are certain domains that are known to be more important than others such as the TATA box and the start codon which are may be crucial to the creation of a properly functioning protein. However, there are numerous other locations within the sequence that may or may not be able to tolerate variation, and to list all would be a pointless exercise, as it is well known in the art which substitutions will form different amino acids and the overall effect of a substituted amino acid on structure.

Furthermore, one of skill in the art would be able to readily conclude that the present invention may be used to detect insertions, deletions, mismatches, mutations and single length polymorphisms. As mismatches are already disclosed in the present specification on pages 38-39, Applicants respectfully submit that the claims are enabled for deletions, insertions, mismatches, mutations and single length polymorphisms. One of skill in the art could readily determine if these deletions, insertions, mismatches, mutations and single length polymorphisms affect the functionality of the sequence in an assay. Accordingly, Applicants respectfully

submit that claims are enabled. Therefore, reconsideration of the rejection to these claims is respectfully requested.

Accordingly, Applicants respectfully ask for reconsideration and withdrawal of the 35 U.S.C. § 112 rejections to claims 1-9 and 36.

VI. Claim Rejections – 35 U.S.C. § 102

Claims 1, 2, and 36 are rejected under 35 U.S.C. § 102 as allegedly being anticipated by Marra et al. Applicants respectfully disagree with this assessment for the reasons set forth below.

Case law holds and the M.P.E.P. states that a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Brothers v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Furthermore, the identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The cited art fails to disclose the subject matter contained in the claims of the present invention.

The Marra reference fails to encompass all elements of any of the claims. The Office Action alleges that Marra discloses a nucleic acid with 99.5% identity² to SEQ ID NO: 1 of this application. Applicants note that the Marra oligonucleotide hybridizes to the GLUT10 sequence from nucleotide 3816 to nucleotide 4366. Applicants additionally note that the claimed sequences are not merely for an isolated nucleic acid, but specifically recited they are for "[a]n isolated nucleic acid *encoding* a glucose transporter protein." (Claim 1). Although the oligonucleotide disclosed by Marra may be said to be part of the mRNA of a glucose transporter, this oligonucleotide does not actually encode a glucose transporter. It is generally accepted that the only portion of a sequence that encodes a protein are the nucleotides located between the start and the stop codons, as this is the only portion that is translated into a protein. The Marra sequence binds in the 3' untranslated region (UTR), which is approximately 2,000 base pairs subsequent to the stop codon. Because the Marra sequence does not coincide with a coding portion of a glucose

² The Office Action quotes a 99.5% identity. However, using the PAIRWISE BLAST program at <http://www.ncbi.nlm.nih.gov/blast/bl2seq/bl2.html>, applicant has only been able to attain 92-97% identity between the two sequences.


transporter, it cannot properly be said to encode a glucose transporter, and therefore does not disclose each and every elements of the claims. Therefore, there can be no finding of anticipation.

Accordingly, Applicants respectfully request that the 35 U.S.C. § 102(b) rejection to claims 1-2 and 36 be withdrawn.

CONCLUSION

In view of the amendments and remarks presented herein, Applicants respectfully submit that the claims in the instant application define patentable subject matter. If questions should remain after consideration of the foregoing, the Examiner is kindly requested to contact Applicants' attorney at the address or telephone number given herein.

Respectfully submitted,


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PATENT TRADEMARK OFFICE

Enclosures: Version With Markings to Show Changes Made

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231, on September 6, 2002.


Susan E. Freedman

Date of Signature: September 6, 2002

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

A marked up version of each of the presently amended claims, highlighting the changes thereto, follows:

36. (Amended) An isolated oligonucleotide that hybridizes to [a] the isolated nucleic acid according to claim 1.